PHARMACEUTICAL PROSPECTS OF THE MANGROVE *HERITIERA FOMES*: A REVIEW

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Abstract:

Mangroves form unique plant communities along the coastal and estuarine areas as they have special adaptations to survive and thrive in hostile, salty environments. They are known to produce an array of secondary metabolites which have attracted the attention of scientists worldwide for exploring their bioactivities. *Heritiera fomes* Banks (family Malvaceae) is a mangrove that has a dense, local distribution in the parts of Indian sub-continents and South East Asia. This mangrove has numerous local applications. Its parts are used as timber in furniture and boat-building industries and by the traditional healers to treat diabetes, gastro-intestinal disorders, skin diseases and so on. Like other mangroves, *H. fomes* is well known for producing a variety of phytochemicals. Extracts and compounds isolated from it have exhibited impressive biological activities. An attempt has been made to compile the up-to-date information on this mangrove plant from scientific databases. This review could serve as an authentic basis for formulating the proposed application of this easily found mangrove in standard as well as complementary medicine.

Keywords: mangroves, pharmacognosy, ethno-medicine, bioactivities, phytomedicine

Introduction:

Natural products have been playing a significant role in traditional ethno-medicine. Phytochemicals are unique compounds, comprising mainly of secondary metabolites that are derived from plants. They have served as a key source of lead molecules in various drug discovery programmes (Murugan *et al.*, 2021).

Mangroves are plants blessed with special ability to tolerate harsh, saline habitats. They not only survive in such hostile environment but also give rise to enormously productive communities. They have numerous applications and their therapeutic importance has been well documented (Bandaranayake, 2002; Manohar, 2021; Nabeelah Bibi *et al.*, 2019).

Heritiera fomes Banks is an important member of mangrove community. It is commonly found mangrove along the coastal lines of South East Asian countries like Myanmar, Malaysia, Thailand and forests of Sundarbans and Bhitarkanika in Bangladesh and India (Giesen *et al.,* 2006). In fact, the name Sundarban, literally meaning "beautiful forest" is believed to be derived from Sundari or Sundri (*Heritiera fomes*), one of the most abundant tree species found in this forest (Naskar, 2004). Forming a vast ecosystem, it supports a variety of fauna; acts as a defensive barrier against natural calamities such as floods and tsunamis; and also prevents the soil erosion.

This mangrove has been widely used by the locals in the ethno-medicine to treat a number of health-ailments. Therefore, the present review would compile latest, up-to-date information about studies done to delineate the pharmaceutical potential of *H. fomes*.

Taxonomy and classification

This mangrove species is taxonomically classified as follows:

Kingdom: Plantae
Sub-kingdom: Viridiplantae
Infra-kingdom: Streptophyta
Phylum: Tracheophyta
Sub-phylum: Spermatophytina
Class: Magnoliopsida
Super-order: Rosanae
Order: Malvales
Family: Malvaceae
Genus: *Heritiera*
Species: *Heritiera fomes*

There lies ambiguity when it comes to classifying *H. fomes* into a family. Many researchers continue to include it in Sterculiaceae family as *H. fomes* Buch. Ham. However, as per the World Mangrove Database, its classification is now revised as *H. fomes* Banks (Malvaceae family). Other mangrove members from the genus *Heritiera* include *H. littoralis* Aiton, *H. macroptera* Kosterm, *H. kanikensis* Majumdar & Banerjee, *H. globosa* Kosterm, and *H. peralata* Kosterm. (Dahdouh-Guebas 2024, World Mangrove database website link)

It is identified by the local names such as *Sundari / Sundri* in the Sundarban forests by Bangla speaking native people, as *Bada Sundari* in Bhitarkanika forest of Odisha state and as *Kanazo* in Myanmar (former Burma) (Anonymous, 2023; Giesen *et al.,* 2006).

Botany:

H. fomes is a Medium-sized evergreen tree that grows up to 25 m, and has numerous erect, pointed, peg-like pneumatophores (around 50 cm long). The trunk is straight, has a rough surface, and is brown in colour. The leaves are of alternate, simple type, dark greenish in colour and have a 1 cm long petiole. Leaf blade is elliptic-lanceolate in shape, is pointed, thick and hard, about 10-20 cm by 5-10 cm. Upper surface appears pale green in colour and is smooth, lower surface is whitish grey and feels rough, having very short, scurfy hair and a net-like venation. Flowers are present in clusters. They are pendulous and are much branched. Flowers are unisexual in *H. fomes*. They are small, cream-orange coloured to pale brownish, having a 6 mm, flower stalk. The number of sepals present is generally 4-5, appear cup-shaped, having a tube beneath, with 4-5 lobes. Calyx lobes are ovate, pointed, hairy, having leathery surfaces on both internal and external sides. Petals are not present. The male flower in *H. fomes* shows the presence of 5 stamens which are fused together. The female flower generally has 4 carpels which are loosely attached and are 2-3 mm long. The style is terminal, long, white but turns brown in colour post maturity. The fruit is sized 2 to 4 cm and appears as a cluster of woody, and winged ripe carpels, which on peeling, it looks knob like having a ventral ridge underneath, and a transverse cum circular ridge. Germination is of hypogeal type. Flowering and fruiting period slightly varies from region to region. In Sundarbans, flowering takes place from May to October whereas in Bhitarkanika, it blooms from March to August. Fruiting is generally observed from May to August. Seeds are solitary and do not exhibit vivipary, but are buoyant, helping in their dispersal (Anonymous, 2023; Giesen *et al.*, 2006; Tomlinson, 1986)

Habitat and distribution

H. fomes is a species that is often seen growing along the landward edges of mangrove forests away from the direct seawater and along brackish tidal streams. It prefers lower salinity. Regions with heavy annual rainfall of 1600 mm to 5334 mm and a warm equable climate of 7.22 °C to 37.78 °C are considered to be conducive for the growth of this species. It prefers well drained soil and grows prolifically in areas where fresh water supply is abundant.

Local and ethno-medicinal uses

A perusal of literature indicates that *H. fomes* has numerous medicinal applications. A decoction is prepared from seeds and leaves to treat various gastro-intestinal disorders such as indigestion, constipation, diarrhoea, dysentery, bloating, colic acidity and lack of appetite (Mollik *et al.*, 2010). Piles are treated using wood powder (Parikh & Datye, 2003). A paste prepared from the bark and stem is applied for curing skin diseases such as eczema, scabies, boils, scars, dermatitis, rashes etc. (Nawaz *et al.*, 2009). Hot decoction of bark is used against diabetes and goitre (Ali *et al.*, 2011; Thatoi & Patra, 2013). Traditional health practitioners use it

to cure fever and pain. Twigs are chewed to clean the teeth (Rahmatullah *et al.,* 2010). Local community has been using the wood of *H. fomes* is for building boats, making poles, and for other construction purpose also as fuel (Giesen *et al.,* 2006). Seed is consumed only in emergency in case of food scarcity. Fish poison is prepared by tribals using bark and roots. Pickle is also made from fruits as a supplementary food (Das, 2020; Mahmud *et al.,* 2014).

Phytochemistry

Both primary and secondary metabolites have been identified from different parts and extracts of *H. fomes* (Table 1). Majority studies have focussed on qualitative analysis to detect different phytochemical classes, and carbohydrates, proteins, fats, reducing sugars, vitamins, minerals, alkaloids, glycosides, anthraquinones, saponins, phenols, flavonoids, steroids, tannins and terpenoids, gums and resins have been reported by various researchers (Feda, 2022; Hossain *et al.,* 2013; Patra & Thatoi, 2015; Ripa *et al.,* 2022; Tabassum, 2020).

Table 1: Quantitative phytochemical contents in *H. fomes* leaf & stem (Patra & Thatoi, 2015)

	Leaf	**Stem**
Primary metabolites		
Carbohydrates	6.45	10.38
Proteins	8.31	9.13
Secondary metabolites		
Phenol	2.47	2.25
Flavonoid	1.88	1.48
Tannin	2.4	2.13
Alkaloid	1.88	1.26
Saponin	15.2	10.8
Vitamins		
Thaimine	0.184	0.203
Riboflavin	0.028	0.027
Minerals		
Nitrogen content	1.33	1.46
Phosphate content	0.07	0.08
Potassium content	1.00	0.99
Values in % dry weight		

Composition of chlorophyll a, chlorophyll b, carotenoids, polyphenols, tannins and proteins has been identified from the leaves (Basak *et al.,* 1996). Bark has been found to be rich

in tannins (Naskar & Guhabakshi, 1987). Proanthocyanidins, a class of polyphenols are present in higher amounts in stem and bark (Dang *et al.*, 2007; Patra & Thatoi, 2015). Flavonol such as epicatechin and phytosterols such as β-sitosterol, stigmasterol, and stigmast-4-en-3-one have been also reported from *H. fomes* extract (Wangensteen *et al.*, 2009). Three unique compounds viz. 2, 5-Anhydrogluconic acid, aminopyrine, and palmitic acid were identified from the root exudates of *H. fomes* using paper chromatography followed by GC-MS (Kumar *et al.*, 2009). Quercitrin-like flavonoid derived glycosides with anti-diabetic activities were identified in the hot water extract of *H. fomes* (Ansari *et al.*, 2022).

Proximate composition and nutrient analysis of *H. fomes* fruits was studied by Hosen *et al.*, (2020). Researchers reported that the fruits are a rich source of proteins, lipids, and vitamin C along with some important micro-nutrients (Table 2).

Table 2: Analysis of nutrients from *H. fomes* fruits (Hosen *et al.*, 2020)

Nutrient / Element / Mineral	**Concentration**
Carbohydrates	8.7 %
Proteins	18.6 %
Lipids	3.1 %
Vitamin C	87.7 mg AA/ 100 g powder
Ca	52.3 mg/kg powder
Cu	10.4 mg/kg powder
Fe	83.8 mg/kg powder
Mg	332.2 mg/kg powder
Mn	8.4 mg/kg powder
P	953.5 mg/kg powder
Zn	10.3 mg/kg powder
K	15.3 g/kg powder
Na	1.3 g/kg powder

Pharmacological activities

Antibacterial

Pneumatophore-extracts prepared in ethanol showed encouraging activity against the tested bacterial strains with zones of inhibitions being greater than 10 mm against majority. *Enterobacter aerogenes* was found to be the most susceptible with a zone of inhibition recorded at 21 mm. (Mondal *et al.*, 2008). The ethanol bark extract was found to be antibacterial in nature when tested against *S. aureus, K. rhizophilia, B. subtilis* and *P. aeruginosa* (Wangensteen *et al.*,

2009) *H. fomes* methanol: ethanol 1:1 fruit extract exhibited relatively weaker anti-bacterial activity against *E. coli*, *Klebsiella* sp., *Shigella boydii*, *S. sonnei*, and *S. aureus* (Hosen *et al.*, 2021). Silver and zinc oxide nano-particles synthesized from the aqueous extracts of *H. fomes* reported zone of inhibition in the range of 9 to 16 mm against the tested pathogenic bacteria (Thatoi *et al.*, 2016). Ethyl acetate extracts of different parts showed highest antibacterial activity against *Shigella dysenteriae* and *Shigella boydii* (Tabassum, 2020). Moderate antibacterial activity of extracts prepared in different solvents has been also reported by Patra & Thatoi (2015) and in acetone by Kalyani *et al.*, (2020).

Antifungal

Weak antifungal activity of methanol and aqueous leaf extracts of *H. fomes* was observed against *Candida kruzii* and *Fusarium* sp. (Patra & Thatoi, 2015).

Anti-oxidant

Wangensteen *et al.*, (2009) reported a promising DPPH radical scavenging and 15-lipoxygenase inhibitory activity and attributed it to the procyanidins present in the ethanol bark extract of *H. fomes*. Hosen *et al.*, (2020) reported high antioxidant activity of *H. fomes* fruit extract with 86.6% DPPH scavenging at 50 µg powder /ml and a reducing power OD of 1.87. Total antioxidant capacities were observed at 102.1 mg GAE/ g powder and 75.9 mg AAE/g powder. Moderate *in vitro* activity of extracts prepared in different solvents has been reported by Patra & Thatoi (2015) with antioxidant capacity recorded between 41.31 to 175.89% dry weight basis. Leaf methanol exhibited the most potent antioxidant activity. Uddin *et al.*, (2004) reported moderate antioxidant potential with free radical scavenging activity RC_{50} values of 2.5 X 10^{-2} and 8.1 X 10^{-3} mg/ml for leaf ethanol and bark ethanol extracts respectively. Synthesized silver and zinc oxide nanoparticles exhibited moderate free radical scavenging activities (Thatoi *et al.*, 2016). Leaf and bark extracts prepared in acetone showed impressive antioxidant activity with IC_{50} values of 26.30 µg/mL and 22 µg/mL respectively (Kalyani *et al.*, 2020). DPPH radical scavenging assay showed encouraging IC_{50} values of 82.24 and 124.98 µg/ml for ethanol bark and leaf extracts respectively. A strong correlation was recorded between total phenolic and flavonoid content and antioxidant capacities (Islam *et al.*, 2019). Pneumatophore ethanol extract was found to have high antioxidant activity with scavenging capacity SC_{50} values of 49 µg/ml and 87 µg/ml for DPPH radical scavenging assay and hydrogen peroxide radical scavenging assay respectively (Sultana *et al.*, 2022).

Analgesic

Ethanol extract prepared using leaves and roots of *H. fomes* was found to have *in vivo* analgesic (pain relieving) activity at par with the standard drug indomethacin. Percentage (%)

inhibition of induced pain in mice was recorded at 84.67 and 83.54 for leaves and roots extracts respectively (Alam, 2022).

Anti-inflammatory

Silver and zinc oxide nano-particles prepared from the aqueous extracts were found to have promising anti-inflammatory activity of approximately 69% and 79% respectively (Thatoi *et al.,* 2016). In another *in vitro* study, bark and leaf ethanol extracts of *H. fomes* indicated their anti-inflammatory potential by inhibiting the haemolysis of erythrocytes. This was further vindicated by an *in vivo* study which showed a 44% decrease in mice paw oedema after they were administered with the plant extract (Islam *et al.,* 2019).

Anti-nociceptive

It a process involving blocking the detection of pain stimulus. Methanol bark extract and ethanol leaf extract were reported to have *in vivo* anti-nociceptive activity (Ali *et al.,* 2011; Hossain *et al.,* 2013)

Anti-diarrhoel

Fruit extract prepared in 1:1 methanol : ethanol at a dosage of 250 mg/Kg of body weight was found to be anti-diarrhoel in nature as it drastically inhibited diarrhoea in tested mice (induced with castor oil administration) (Hosen *et al.,* 2021).

Anti-diabetic

Ansari *et al.,* (2022) reported significant improvement in glucose tolerance and in plasma insulin releasing response. Hot aqueous extract of *H. fomes* was tested *in vitro* and *in vivo*. Significant reduction in glucose absorption was observed in rats which were orally administered with the extract. Sarkar *et al.,* (2019) reported promising *in vitro* anti-diabetic activity of leaf extract based on the inhibitory capacity of enzyme α-amylase, transport of glucose molecules across yeast cells and increased glucose adsorption capacity. *In vivo* anti-hyperglycaemic activity of methanol bark extract has been reported. A significant reduction in the glucose concentrations in serum was recorded after 60 and 90 min of dose administration at 250 and 500 mg/kg body weight (Ali *et al.,* 2011). Synthesized silver and zinc oxide nanoparticles exhibited moderate α-amylase inhibitory potential (Thatoi *et al.,* 2016). Ethanol extract of leaves, bark, and roots exhibited highly promising hypoglycaemic activity when administered in alloxan-induced diabetic Swiss albino mice at 200 and 400 mg/kg body weight (Feda, 2022). Ethanol extract of pneumatophores was also found to have significant *in vivo* anti-hyperglycaemic activity when tested in streptozotocin-induced diabetic rats (Sultana *et al.,* 2022).

Anti-arthritic

It is measured with respect to percentage inhibition of Bovine serum protein denaturation by BSA method. More the % inhibition, more the activity. Leaf ethanol, root chloroform, and

bark ethanol extracts of *H. fomes* showed moderate yet promising (being crude extracts) anti-arthritic efficacy with 49.49%, 49.06%, and 47.83% respectively as compared to 96.91% by the standard diclofenac sodium (Eusufzai *et al.,* 2020). In another *in vitro* study, 63.28% protein inhibition by chloroform root extract was reported by Ripa *et al.,* (2022).

Anti-obesity

Mirza *et al.,* (2017) orally administered leaf methanol extract to high fat cafeteria diet (HFCD) fed obese wistar rats and observed significant lowering of physic-chemical parameters such as gained body and organ weight, cholesterol, triglycerides and glucose levels. Elevated enzymatic liver markers due to induced obesity also resumed their normal levels post treatment with *H. fomes* extract. Overall results of this *in vivo* study clearly highlighted the anti-obesity potential of *H. fomes*.

CNS depressant

Central Nervous System depressant activity of *H. fomes* in mice models was studied (Taslim, 2022). The ethanol extract of *H. fomes* given at a dose of 250 mg/kg and 500 mg/kg significantly reduced the locomotor activity of mice when analyzed using open field and hole-cross tests as compared to the control distilled water and the commercial drug diapzepam. Statistically significant increase in immobility time force was recorded after the administration of plant extract.

Thrombolytic

Leaf, root, bark extracts prepared using ethanol, petroleum ether, chloroform, and ethyl acetate showed noteworthy thrombolytic activity with clot lysis percentage ranging of 14.55 to 22.98%. Leaf petroleum ether extract was observed with highest activity of 22.98% which was not very less than 24.05% exhibited by the standard clopidogrel (Eusufzai *et al.,* 2020). Ripa *et al.,* (2022) also reported moderate thrombolytic activity of different *H. fomes* extracts/fractions with highest % clot lysis of around 33.12 shown by ethanol leaf extract as compared to 67.77% exhibited by the standard streptokinase.

Cytotoxic

Bark extract showed no cytotoxic effect when analysed through the brine shrimp lethality assay (Wangensteen *et al.,* 2009). However, Hosen *et al.,* (2021) reported a promising cytotoxicity of the fruit extract with IC_{50} value of 74.1 µg/ml. Leaf chloroform and bark methanol extracts had shown LC_{50} values of 234.77 and 47.09 mg/ml respectively against *Artemia salina* naupli (Rahmatullah *et al.,* 2010). Weak cytotoxicity of extracts prepared from different parts was also reported by Tabassum (2020). Chloroform was found to demonstrate relatively higher mortality rate than other extracts.

Anticancer

Anticancer activity of leaf and stem methanol extract was reported by Patra & Thatoi (2013). A 40% inhibition of B16 mouse melanoma with IC_{50} values of 75 and 100 µg/ml was observed in the *in vitro* experiment whereas experiments done in the Swiss albino mice showed an inhibition of 41% against Ehrlich Ascites Carcinoma (EAC).

Anthelmintic and insecticidal

Petroleum ether, chloroform, and ethyl acetate soluble fractions of ethanol extract prepared from leaf, bark, and root of *H. fomes* were tested against Helminth *Pheretima posthuma* and notorious pest beetle *Tribolium castaneum*, respectively. All the tested extracts showed a promising anthelmintic activity at concentrations of 25–75 mg/mL and resulted in the paralysis and death of earthworms in comparison with standard chemical albendazole. The ethanol bark extract was found to be the most potent. In case of insecticidal test, leaf ethanol extract exhibited the most lethal mortality rate (73%) (Ripa *et al.*, 2022)

Conclusion:

The present review clearly highlights the pharmaceutical potential of mangrove *H. fomes* as indicated by the diverse range of bioactivities showcased by this plant. More emphasis has to be given on the isolation of novel bioactive compounds from this plant which would have far potent activities than the crude and un-purified extracts.

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